NICE advice

Type 2 diabetes mellitus: medicines optimisation priorities

Key therapeutic topic

Published: 15 January 2015
nice.org.uk/guidance/ktt12

Options for local implementation

- The NICE guideline on type 2 diabetes in adults: management recommends adopting an individualised approach to diabetes care. Involve people with type 2 diabetes in decisions about their individual glycated haemoglobin (HbA1c) target, and reassess their individual needs and circumstances at each review. Consider stopping any medicines that are not effective.
- Consider carefully, with an individualised approach, the benefits and risks of controlling blood glucose and the use of blood glucose lowering medicines. Review and, if appropriate, optimise prescribing to ensure that it is in line with NICE guidance taking into account the person's preferences, comorbidities, risks from polypharmacy, and their life expectancy and consequent chances of benefiting from long-term interventions.
- When choosing and reviewing medicines, take into account the person's individual clinical circumstances, preferences and needs; the medicines' efficacy (based on metabolic response), safety and tolerability; and the licensed indications or combinations available. Consider also the cost of medicines: the NICE guideline recommends choosing medicines with the lowest acquisition cost if 2 in the same class are appropriate.
- The NICE guideline recommends that self-monitoring of blood glucose levels for adults with type 2 diabetes should not routinely be offered. See the guideline for details on when self-monitoring is appropriate.

Evidence context

Type 2 diabetes is a chronic metabolic condition characterised by insulin resistance and insufficient pancreatic insulin production, resulting in high blood glucose levels. Type 2 diabetes is commonly associated with obesity, physical inactivity, raised blood pressure and disturbed blood lipid levels, and therefore is recognised to have an increased cardiovascular risk. It is associated with long-term microvascular and macrovascular complications, together with reduced quality of life and life expectancy. The NICE guideline on type 2 diabetes in adults: management recommends adopting an individualised approach to diabetes care, which takes into account personal preferences, comorbidities, risks from polypharmacy, and the ability to benefit from long-term interventions because of reduced life expectancy. Such an approach is especially important in the context of multimorbidity. See also the key therapeutic topic on multimorbidity and polypharmacy for further information on reviewing polypharmacy and de-prescribing.

The guideline recommends that the person's needs and circumstances should be reassessed at each review and consideration given to stopping any medicines that are not effective. Controlling blood glucose levels requires a careful balance between the intensity of the treatment regimen and avoiding hypoglycaemia. This key therapeutic topic focusses on blood glucose management; however, the NICE guideline also has recommendations on patient education, dietary advice, blood pressure management, antiplatelet therapy and management of complications. Recommendations on the management of blood lipids in people with type 2 diabetes are given in the NICE guideline on cardiovascular disease: risk assessment and reduction, including lipid modification. All these components should be given due consideration in the care of people with type 2 diabetes.

The NICE pathway on diabetes brings together all related NICE guidance and associated products in a set of interactive topic-based diagrams. NICE has also published a quality standard on diabetes in adults, which provides a concise set of prioritised statements designed to drive measurable quality improvements within this area. In September 2016, the Care Quality Commission published My diabetes, my care a community diabetes care review that considers how well care services work together to deliver high-quality diabetes care. The review makes a number of recommendations for how health and social care commissioners, providers and professionals could work together to improve diabetes care and prevention.

Target blood glucose levels

The NICE guideline on type 2 diabetes in adults: management recommends that people with type 2 diabetes should be involved in decisions about their individual glycated haemoglobin (HbA1c) target and be supported to achieve and maintain this. For adults with type 2 diabetes that

is managed either by lifestyle and diet, or by lifestyle and diet combined with a single drug not associated with hypoglycaemia, the guideline recommends supporting the person to aim for an HbA1c level of 48 mmol/mol (6.5%). For adults on a drug associated with hypoglycaemia, the recommended aim is an HbA1c level of 53 mmol/mol (7.0%). If HbA1c levels are not adequately controlled by a single drug and rise to 58 mmol/mol (7.5%) or higher, advice about diet, lifestyle and adherence to drug treatment should be reinforced, the person should be supported to aim for an HbA1c level of 53 mmol/mol (7.0%) and drug treatment should be intensified (taking into account principles of individualised care). When intensification of drug treatment is required the guideline recommends that additional treatments should be introduced in a stepwise manner, checking for tolerability and effectiveness of each drug.

The target HbA1c level can be relaxed on a case-by-case basis, with particular consideration for people who are older or frail, those with a reduced life expectancy, those for whom tight blood glucose control poses a high risk of the consequences of hypoglycaemia, and those for whom intensive management would not be appropriate, such as people with significant comorbidities. The NICE patient decision aid for adults with type 2 diabetes can support the implementation of the guideline recommendations on the individualised agreement of HbA1c targets.

The Quality and Outcomes Framework (QOF) allocates points for achieving 3 levels of glucose control in people with type 2 diabetes: HbA1c of 75 mmol/mol (9%) or less, 64 mmol/mol (8%) or less and 59 mmol/mol (7.5%) or less.

What are the benefits and risks of controlling blood glucose?

The NICE guideline included a review question comparing intensive glycaemic control with conventional glycaemic control in people with type 2 diabetes (see the full guideline for details). This used a Cochrane review (Hemmingsen et al. 2013 [CD008143]) as the primary source of evidence because it included all relevant randomised controlled trials (RCTs). The Cochrane review included 28 RCTs in 34,912 people with type 2 diabetes; the NICE guideline excluded 8 RCTs in which intensive and conventional glycaemic control groups had significant baseline differences in adjunctive treatment for cardiovascular risk factors.

Compared with conventional control, the NICE guideline found that intensive glycaemic control did not statistically significantly reduce death from any cause (relative risk [RR] 0.98, 95% confidence interval [CI] 0.88 to 1.09; 16 RCTs, n=6504) or death from cardiovascular causes (RR 1.15, 95% CI 0.98 to 1.35; 14 RCTs, n=6356). No statistically significant effect of targeting intensive glycaemic control was found on the composite of macrovascular complications (RR 0.98, 95% CI 0.74 to 1.30; 8 RCTs, n=5334), non-fatal myocardial infarction (RR 0.92, 95% CI 0.78 to 1.09;

9 RCTs, n=5902), congestive heart failure (RR 0.82, 95% CI 0.62 to 1.08; 8 RCTs, n=5460), non-fatal stroke (RR 1.06, 95% CI 0.80 to 1.41; 8 RCTs, n=5488) or amputation of lower extremity (RR 0.73, 95% CI 0.42 to 1.25; 7 RCTs, n=5079).

Intensive glycaemic control did reduce the risk of the composite of microvascular complications (RR 0.75, 95% CI 0.61 to 0.92; 3 RCTs, n=4376), but no statistically significant reductions in risk were seen for the individual end points of nephropathy (RR 0.64, 95% CI 0.32 to 1.29; 7 RCTs, n=4754), progression to end-stage renal disease (RR 0.94, 95% CI 0.47 to 1.89; 4 RCTs, n=4803) or retinopathy (RR 0.79, 95% CI 0.56 to 1.11; 5 RCTs, n=4614).

Intensive glycaemic control increased the risk of severe hypoglycaemia (RR 2.23, 95% CI 1.22 to 4.08; 13 RCTs, n=5452) and mild hypoglycaemia (RR 1.85, 95% CI 1.53 to 2.25; 12 RCTs, n=6320). The guideline development group agreed overall that there was evidence to support the setting of target values, but considered it important to ensure that a person's risk of hypoglycaemia is evaluated when setting appropriate target levels.

Self-monitoring of blood glucose

The NICE guideline on type 2 diabetes in adults: management recommends that self-monitoring of blood glucose levels for adults with type 2 diabetes should not routinely be offered unless:

- the person is on insulin treatment or
- there is evidence of hypoglycaemic episodes or
- the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery or
- the person is pregnant, or is planning to become pregnant (see the NICE guideline on diabetes in pregnancy for more information).

Healthcare professionals should also take the Driver and Vehicle Licensing Agency (DVLA) guidance Assessing fitness to drive guide into account when offering self-monitoring of blood glucose levels to people with type 2 diabetes and advise them about their own particular requirements.

The guideline development group discussed the evidence for self-monitoring of blood glucose and concluded that overall, while a statistically significant difference was observed in HbA1c levels in favour of self-monitoring, this was not clinically meaningful and was unlikely to be cost-effective.

The reduction in HbA1c levels with self-monitoring was 2 mmol/mol (0.22%), which was less than 5 mmol/mol (0.5%), the agreed threshold for minimal important difference.

The guideline recommends considering short-term self-monitoring of blood glucose levels in adults with type 2 diabetes (and reviewing treatment as necessary) when starting treatment with oral or intravenous corticosteroids or to confirm suspected hypoglycaemia. It is also recommended for health professionals to be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia, and reviewing treatment as necessary.

The guideline recommends that if adults with type 2 diabetes are self-monitoring their blood glucose levels this should be assessed in a structured way at least annually, assessing various issues including the impact on the person's quality of life and the continued benefit of self-monitoring.

Blood glucose lowering therapy

The NICE guideline on type 2 diabetes in adults: management recommends that the choice of medicine for managing blood glucose levels should be made following a discussion with the individual person about the benefits and risks of drug treatment, and the options available. The guideline recommends an individualised approach to treatment choice taking into account the person's individual preferences and needs, and their individual clinical circumstances, for example, comorbidities and risks from polypharmacy. Choice should also take into account the medicine's efficacy (based on metabolic response), safety and tolerability; and the licensed indications or combinations available. Cost should be taken into account and the guideline recommends choosing medicines with the lowest acquisition cost if 2 in the same class are appropriate. The NICE patient decision aid for adults with type 2 diabetes can support the implementation of the guideline recommendations on the pharmacological management of blood glucose.

Efficacy

Although all blood glucose lowering medicines are effective (at a population level) in reducing HbA1c levels, clinical outcome data, particularly around cardiovascular outcomes, are limited. Improvements in surrogate markers (including HbA1c levels) do not automatically confer benefits on mortality or morbidity, and risks may only become apparent over time when medicines are used widely in a diverse population.

Metformin, sulfonylureas and insulin have outcome data from the UK Prospective Diabetes Study (UKPDS). In UKPDS 33 (UKPDS Group 1998), intensive glycaemic control with sulfonylureas or insulin compared with conventional control (median HbA1c after 10 years follow up: 53 mmol/mol

[7.0%] compared with 63 mmol/mol [7.9%]) reduced the risk of microvascular complications, but not macrovascular disease. In UKPDS 34 (UKPDS Group 1998) in people who were overweight or obese, intensive glycaemic control with metformin compared with conventional control (median HbA1c after 10.7 years follow up: 57 mmol/mol [7.4%] compared with 64 mmol/mol [8.0%]) reduced the risk of MI and death from any cause. Long-term follow-up of UKPDS (Holman et al. 2008) found a continued reduction in microvascular risk and emergent risk reductions for MI and death in the sulfonylurea-insulin group and a continued benefit for risk of MI and death in the metformin group.

Other blood glucose lowering medicines have not shown such cardiovascular benefits in people with type 2 diabetes. For example, in PROACTIVE (Dormandy et al. 2005), pioglitazone did not reduce the composite primary end point of death from any cause, non-fatal MI, stroke, acute coronary syndrome, major leg amputation, coronary revascularisation and leg revascularisation in people with type 2 diabetes and pre-existing major macrovascular disease, but did increase the incidence of oedema, weight gain and heart failure. In SAVOR–TIMI 53 (Scirica et al. 2013), saxagliptin did not reduce the composite primary end point of cardiovascular death, MI, or ischemic stroke, but did increase the risk of admission to hospital because of heart failure in people with type 2 diabetes who had established cardiovascular disease, or were current smokers, or had dyslipidaemia or hypertension. (See the medicines evidence commentary on type 2 diabetes: study finds no benefit from saxagliptin on cardiovascular outcomes.) In EXAMINE (White et al. 2013) alogliptin did not reduce the composite primary end point of death from cardiovascular causes, non-fatal MI or non-fatal stroke in people with type 2 diabetes who had had a recent acute coronary syndrome. (See the medicines evidence commentary on type 2 diabetes: study finds no benefit from alogliptin on cardiovascular outcomes in people with a recent acute coronary syndrome). Similarly, in TECOS (Green et al. 2013) sitagliptin did not reduce the composite primary end point of death from cardiovascular causes, non-fatal MI, non-fatal stroke, or hospital admission for unstable angina in people with type 2 diabetes who had established cardiovascular disease.

More recently 2 outcome studies have shown cardiovascular benefits with blood glucose lowering medicines. In EMPA-REG OUTCOME (Zinman et al. 2015), adding the sodium glucose cotransporter 2 (SGLT-2) inhibitor empagliflozin to standard care in people with type 2 diabetes and established cardiovascular disease reduced the risk of cardiovascular outcomes. The composite end point of death from cardiovascular causes, non-fatal MI or non-fatal stroke was reduced with a number needed to treat of 63 over 3 years (hazard ratio 0.86; 95% CI 0.74 to 0.99). However, this was driven by a reduction in the risk of cardiovascular death, not MI or stroke. See the medicines evidence commentary on type 2 diabetes: study finds empagliflozin reduces adverse cardiovascular outcomes, which discusses this study in more detail.

LEADER (Marso et al. 2016) assessed the cardiovascular effects of the glucagon-like-peptide-1 (GLP-1) mimetic liraglutide as an add-on to standard care in people with type 2 diabetes who had established cardiovascular disease or were at high risk of developing it. Liraglutide reduced the composite end point of death from cardiovascular causes, non-fatal MI or non-fatal stroke with a number needed to treat of 66 over 3.5 years (hazard ratio 0.87; 95% CI 0.78 to 0.97). However, again this was driven by a reduction in the risk of cardiovascular death, not MI or stroke. See the medicines evidence commentary on type 2 diabetes: liraglutide reduces cardiovascular risk in people at high risk of having a cardiovascular event for more details. Another study with the GLP-1 mimetic lixisenatide in a people with recent acute coronary syndrome (ELIXA, Pfeffer et al. 2015), did not show a reduction in cardiovascular events.

The ORIGIN study found that, compared with standard care (non-insulin therapy), the early use of basal insulin glargine for a median of 6 years had no effect on cardiovascular outcomes in people with impaired fasting glucose, impaired glucose tolerance or early type 2 diabetes who also had cardiovascular risk factors. As perhaps expected, episodes of severe hypoglycaemia were more common in people receiving insulin glargine. The incidence of a first episode of severe hypoglycaemia was 1.00 per 100 patient-years with insulin glargine and 0.31 per 100 patient-years with standard care ($p<0.001$) (see the medicines evidence commentary on insulin glargine: no effect on cardiovascular outcomes in early type 2 diabetes for details).

Because patient orientated outcomes are not reported in many studies of blood glucose lowering drugs, the guideline development group for the NICE guideline on type 2 diabetes in adults: management agreed that change in HbA1c would be the main outcome measure to reflect glycaemic control and that a difference of 5 mmol/mol (0.5%) was clinically important.

Safety

The MHRA has highlighted several safety concerns with blood glucose lowering medicines and these are cross referenced in the NICE guideline on type 2 diabetes in adults: management. For example, warnings about pioglitazone and risks of heart failure, bladder cancer and use in older people have been incorporated into the summaries of product characteristics, and the guideline recommends that pioglitazone should not be offered or continued in adults with heart failure, hepatic impairment, diabetic ketoacidosis, bladder cancer or uninvestigated macroscopic haematuria. The MHRA reported in the January 2011 edition of Drug Safety Update that cases of heart failure have been reported when pioglitazone was used in combination with insulin (especially in people with pre-existing risk factors for developing heart failure). If the combination is used, people should be observed for signs and symptoms of heart failure, weight gain, and oedema; and pioglitazone discontinued if any deterioration in cardiac status occurs.

All the glucagon-like-peptide-1 (GLP-1)-based therapies, GLP-1 agonists and dipeptidylpeptidase-4 (DPP-4) inhibitors (gliptins) have warnings in their summaries of product characteristics about a risk of developing acute pancreatitis. In the March 2009 edition of Drug Safety Update, the MHRA drew attention to reports of severe pancreatitis and renal failure associated with exenatide (Byetta), and in the September 2012 edition of Drug Safety Update, reports of acute pancreatitis associated with gliptins.

In the April 2016 edition of Drug Safety Update, the MHRA warned about the risk of diabetic ketoacidosis (DKA) with the SGLT-2 inhibitors canagliflozin, dapagliflozin and empagliflozin. Serious and life-threatening cases of DKA have been reported in people taking SGLT-2 inhibitors and, in several cases, blood glucose levels were only moderately elevated, which is atypical for DKA. When treating people who are taking an SGLT-2 inhibitor the MHRA recommends testing for raised ketones in people with ketoacidosis symptoms, even if plasma glucose levels are near-normal. It advises informing people who are being treated with SGLT-2 inhibitors of the signs and symptoms of DKA and advising them to seek immediate medical advice if they develop any of these. SGLT-2 inhibitors should be discontinued immediately if DKA is suspected or diagnosed. Treatment with SGLT-2 inhibitors should also be interrupted in people who are hospitalised for major surgery or acute serious illnesses.

In the June 2016 edition of Drug Safety Update, the MHRA warned that a signal of increased lower limb amputation with the SGLT-2 inhibitor canagliflozin was being investigated. In the ongoing cardiovascular outcomes trial, CANVAS, the incidence of lower limb amputation (primarily of the toe) is higher in the canagliflozin groups compared with the placebo group.

One possible side effect of blood glucose lowering medicines is hypoglycaemia, and controlling blood glucose needs a careful balance between the intensity of the treatment regimen and avoiding hypoglycaemia. The medicines evidence commentary on type 2 diabetes: increased risk of hypoglycaemia with combined use of dipeptidyl peptidase-4 (DPP-4) inhibitors and sulfonylureas discusses a systematic review and meta-analysis which found that adding a DPP-4 inhibitor to a sulfonylurea increased the risk of hypoglycaemia by around 50%. Many of the summaries of product characteristics for blood glucose lowering medicines warn about the increased risk of hypoglycaemia when combining treatments, particularly with a sulfonylurea or insulin, and a lower dose of insulin or a sulfonylurea may be needed.

Blood glucose lowering therapy

This section outlines recommendations on blood glucose lowering therapy from the NICE guideline on type 2 diabetes in adults: management. See also the algorithm for blood glucose lowering therapy in adults with type 2 diabetes at the end of this section.

Rescue therapy at any phase of treatment

If an adult with type 2 diabetes is symptomatically hyperglycaemic, the NICE guideline recommends considering insulin or a sulfonylurea, and reviewing treatment when blood glucose control has been achieved.

Initial drug treatment

The NICE guideline recommends offering standard-release metformin as the initial drug treatment for adults with type 2 diabetes (or considering a trial of modified-release metformin in people who have had gastrointestinal side effects with the standard-release preparation). If metformin is contraindicated (for example, in people with renal impairment) or not tolerated, the guideline recommends considering initial drug treatment with a DPP-4 inhibitor (gliptin) or pioglitazone or a sulfonylurea. The guideline also advises that repaglinide is both clinically effective and cost effective if metformin is contraindicated or not tolerated in adults with type 2 diabetes. However there is no licensed non-metformin-based combination containing repaglinide that can be offered at first intensification. This subsequent constraint on intensification requires discussion with the individual.

If metformin is contraindicated or not tolerated, SGLT-2 inhibitors are an option in certain circumstances. NICE technology appraisal guidance on canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes recommends monotherapy with an SGLT-2 inhibitor as an option where metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if:

- a DPP-4 inhibitor would otherwise be prescribed and
- a sulfonylurea or pioglitazone is not appropriate.

First intensification of drug treatment

In adults with type 2 diabetes, if initial drug treatment with metformin has not continued to control HbA1c to below the person's individually agreed threshold for intensification, the guideline recommends considering dual therapy with:

- metformin and a DPP-4 inhibitor (gliptin) or
- metformin and pioglitazone or
- metformin and a sulfonylurea or
- metformin and an SGLT-2 inhibitor in certain circumstances.

NICE guidance on treatment with metformin and an SGLT-2 inhibitor is given in NICE technology appraisal guidance on canagliflozin in combination therapy for treating type 2 diabetes, dapagliflozin in combination therapy for treating type 2 diabetes and empagliflozin in combination therapy for treating type 2 diabetes. The SGLT-2 inhibitors in dual therapy with metformin are recommended as options for treating type 2 diabetes, only if:

- a sulfonylurea is contraindicated or not tolerated or
- the person is at significant risk of hypoglycaemia or its consequences.

If metformin is contraindicated or not tolerated and initial drug treatment has not continued to control HbA1c to below the person's individually agreed threshold for intensification, the guideline recommends considering dual therapy with:

- a DPP-4 inhibitor (gliptin) and pioglitazone or
- a DPP-4 inhibitor (gliptin) and a sulfonylurea or
- pioglitazone and a sulfonylurea.

The guideline development group considered that the overall quality of the evidence for first intensification was moderate to low, and the evidence was weighted towards metformin-based combinations. There was limited evidence for treatment intensification options for people for whom metformin is contraindicated or not tolerated. There was strong evidence from the health economic model showing that, when added to metformin, GLP-1 mimetics were not cost effective at first intensification and they were not recommended. The guideline development group noted that where all other dual therapy options were not appropriate, individuals would naturally progress to second intensification where GLP-1 mimetics would become an option in combination with metformin. GLP-1 mimetics were not considered at first intensification in people for whom metformin is contraindicated or not tolerated.

Second intensification of drug treatment

If dual therapy with oral drugs has not continued to control HbA1c to below the person's individually agreed threshold for intensification, the guideline recommends considering either triple therapy with oral drugs or starting insulin-based treatment. For triple therapy the following are recommended:

- metformin, a DPP-4 inhibitor (gliptin) and a sulfonylurea or
- metformin, pioglitazone and a sulfonylurea or
- metformin, pioglitazone or a sulfonylurea, and an SGLT-2 inhibitor in certain circumstances.

NICE technology appraisal guidance on canagliflozin and empagliflozin recommend these drugs as options in triple therapy as above. The NICE technology appraisal guidance on dapagliflozin in triple therapy recommends it is started as an option only in combination with metformin and a sulfonylurea.

If this triple therapy is not effective, not tolerated or contraindicated, the guideline recommends considering combination therapy with metformin, a sulfonylurea and a GLP-1 mimetic for adults with type 2 diabetes who:

- have a BMI of 35 kg/m^2 or higher (adjust accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity or
- have a BMI lower than 35 kg/m^2 and for whom insulin therapy would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.

GLP-1 mimetic therapy should be continued only when people have a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c **and** a weight loss of at least 3% of initial body weight in 6 months).

If metformin is contraindicated or not tolerated, and if dual therapy with 2 oral drugs has not continued to control HbA1c to below the person's individually agreed threshold for intensification, the guideline recommends considering insulin-based treatment. GLP-1 mimetics were not considered here.

The guideline recommends that a GLP-1 mimetic in combination with insulin should be offered only with specialist care advice and ongoing support from a consultant-led multidisciplinary team.

The guideline development group considered that the overall quality of the evidence for second intensification was low.

Insulin-based treatments

The NICE guideline recommends that a structured programme employing active insulin dose titration should be used when insulin therapy is started in adults with type 2 diabetes. Metformin should be continued in people without contraindications or intolerance. The continued need for other blood glucose lowering therapies should be reviewed: use of an SGLT-2 inhibitor in combination with insulin with or without other blood glucose lowering drugs is recommended as an option in NICE technology appraisal guidance.

When insulin therapy is necessary, the guideline recommends that it should be started from a choice of a number of insulin types and regimens. NPH insulin injected once or twice daily according to need is the preferred option. The long-acting insulin analogues, insulin detemir or insulin glargine can be considered as an alternative in certain circumstances (see the guideline for full details), such as if:

- the person needs assistance from a carer or healthcare professional to inject insulin, and use of insulin detemir or insulin glargine would reduce the frequency of injections from twice to once daily or
- the person's lifestyle is restricted by recurrent symptomatic hypoglycaemic episodes or
- the person would otherwise need twice daily NPH insulin injections in combination with oral glucose lowering drugs.

The recommendations for insulin glargine also apply to any current and future biosimilar product(s) of insulin glargine that have an appropriate marketing authorisation that allows the use of the biosimilar(s) in the same indication. For more information on the insulin glargine biosimilar, Abasaglar, see the evidence summary: new medicine publication on diabetes mellitus type 1 and type 2: insulin glargine biosimilar (Abasaglar).

The guideline development group considered that there was strong evidence that insulin degludec was not cost-effective, and this long-acting insulin analogue was not recommended. Short-acting

insulins and pre-mixed (biphasic) insulin preparations are also options in particular circumstances (see the guideline for details).

Several new insulin products have been launched recently and the European Medicines Agency issued a risk minimisation strategy for high-strength and fixed-combination insulin products in October 2015. In the April 2015 edition of Drug Safety Update the MHRA issued advice to health professionals to minimise the risk of medication errors with recently launched high strength, fixed combination and biosimilar insulin products. See the key therapeutic topic on safer insulin prescribing for more information.

Algorithm for blood glucose lowering therapy in adults with type 2 diabetes

This is available as a pdf (Note: NICE technology appraisal guidance on dapagliflozin in triple therapy [TA418] has now been published).

Prescribing data

The Health and Social Care Information Centre report Prescribing for diabetes in England: 2005/6 to 2015/16 found that in the financial year 2015/16 there were 49.7 million items prescribed for diabetes at a net ingredient cost of £956.7 million. This was a 5.3% (2.5 million) rise in the number of items and a 10.1% (£88.0 million) rise in the net ingredient cost from 2014/15. The prescribing of 'other antidiabetic drugs' (which includes the newer blood glucose-lowering drugs) has increased considerably in recent years. The number of items prescribed increased by 256% (5.0 million) from 2005/6 to 2015/16 with a growth in net ingredient cost of 243% (£193.2 million).

The net ingredient cost of all insulin therapy in primary care in 2015/16 was £343.7 million; a growth of 55.6% from 2005/6. In the financial year 2015/16, 1.4 million items of insulin glargine were prescribed at a cost of £80 million, 700,000 items of insulin detemir were prescribed at a cost of £44 million and 43,000 items of insulin degludec at a cost of £4.7 million. This compared with 600,000 items of NPH (isophane) insulin at a cost of £17.5 million.

A medicines optimisation key therapeutic topic (MO KTT) prescribing comparator is available to support this topic – **Long-acting insulin analogues:** the number of prescription items for long-acting human analogue insulins as a percentage of the total number of prescription items for all long-acting and intermediate acting insulins excluding biphasic insulins[1].

- Data for the 3-month period July to September 2016 show a 2.2 fold variation in prescribing rates at Clinical Commissioning Group (CCG) level, from 44.4% to 97.3%.

- Between the 3-month period July to September 2013 and the 3-month period July to September 2016 there was a 4.1% decrease in the comparator value for England (total prescribing) from 81.9% to 78.5%.
- Over the same period there was a 6.8% increase in the variation between CCGs, as measured by the inter-decile range, an absolute increase of 1.8%. The inter-decile range is the difference between the highest and lowest values after the highest and lowest 10% of values have been removed.

The development of further prescribing comparators to support this key therapeutic topic is being explored by the NHS England Medicines Optimisation Intelligence Group[2].

The Medicines optimisation dashboard, which brings together a range of medicines-related metrics from across sectors, includes diabetes metrics related to this key therapeutic topic. These are:

- Diabetes Mellitus (DM009) % achieving upper threshold or above, which is the percentage of practices in a CCG that achieve upper threshold or above (92% or more inclusive of exceptions) for QOF indicator DM009.
- Diabetes Mellitus (DM009) % underlying achievement, which is the percentage underlying achievement at CCG level for QOF indicator DM009 inclusive of exceptions.
- Emergency diabetes admissions, which is the number of emergency attendances for diabetes per 100 patients on the practice QOF diabetes disease register.

The medicines optimisation dashboard helps NHS organisations to understand how well their local populations are being supported to optimise medicines use and inform local planning. The dashboard allows NHS organisations to highlight variation in local practice and provoke discussion on the appropriateness of local care. It is not intended as a performance measurement tool and there are no targets.

[1] The comparators and associated data presented here are based on the previous Key therapeutic topics publication (February 2016). Data provided by the NHS Digital (October 2016; source: Information Services Portal, Business Services Authority). For details of any update to the comparators refer to the NHS Digital website and the Information Services Portal, Business Services Authority.

[2] For details of any update to the comparators refer to the NHS Digital website and the Information Services Portal, Business Services Authority.

Update information

January 2017: This topic was retained for the 2017 update of medicines optimisation: key therapeutic topics. The evidence context has been updated in the light of new guidance and important new evidence.

About this key therapeutic topic

This document summarises the evidence base on this key therapeutic topic which has been identified to support medicines optimisation. **It is not formal NICE guidance.**

For information about the process used to develop the Key therapeutic topics, see the integrated process statement.

ISBN: 978-1-4731-0945-2